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How to use this monograph

This CME activity contains both audio and print components. To receive credit, the participant should listen to the CDs or tapes, review the monograph and complete the post-test and evaluation form. This monograph contains edited comments, clinical trial schemas, graphics and references that supplement the audio program and the website, ProstateCancerUpdate.net, where you will find a full transcription of the audio program and an easy-to-use interactive version of this monograph with links to relevant full-text articles, abstracts, trial information and other web resources indicated here in [red underlined text](#).

Prostate Cancer Update: A CME Audio Series and Activity

Statement of Need/Target Audience

Prostate cancer is one of the most rapidly evolving fields in urology. Published results from clinical trials lead to the emergence of new surgical and radiation therapy techniques and therapeutic agents, along with changes in the indications for existing treatments. In order to offer optimal patient care — including the option of clinical trial participation — the practicing urologist must be well-informed of these advances.

To bridge the gap between research and patient care, Prostate Cancer Update utilizes one-on-one discussions with leading urologic oncology investigators. By providing access to the latest research developments and expert perspectives, this CME program assists physicians in the formulation of up-to-date clinical management strategies.

Issue 4, 2002 of Prostate Cancer Update consists of discussions with four research leaders on a variety of important issues, including antiandrogen withdrawal response, timing and choice of hormonal therapy, extent of pelvic lymphadenectomy, appropriate biopsy algorithms, and effects of androgen deprivation on bone.

Learning Objectives

Upon completion of this activity, participants should be able to:

- Discuss how to use antiandrogen withdrawal as an intervention for prostate cancer patients progressing on combined androgen blockade.
- Explain the rationale for monitoring patients with elevated PSAs and two negative biopsies, rather than obtaining further biopsies.
- Compare the treatment trends in CaPSURE to one's own management of prostate cancer patients.
- Describe how to counsel prostate cancer patients about the timing and choice of hormonal therapy.
- Explain the staging and therapeutic implications of extended pelvic lymphadenectomy in patients undergoing radical prostatectomy.
- Identify the effects of androgen deprivation therapy on bone and possible interventions in prostate cancer patients.
- Review the relationship between obesity and race in predicting adverse pathologic variables in patients undergoing radical prostatectomy.

Accreditation Statement

This activity has been planned and implemented in accordance with the Essential Areas and Policies of the Accreditation Council for Continuing Medical Education (ACCME) through the joint sponsorship of the Postgraduate Institute for Medicine and NL Communications, Inc. The Postgraduate Institute for Medicine is accredited by the ACCME to provide continuing medical education for physicians.

Credit Designation Statement

The Postgraduate Institute for Medicine designates this educational activity for a maximum of 3 hours in category 1 credit toward the AMA Physician's Recognition Award. Each physician should claim only credits that he/she actually spent in the activity.

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The Postgraduate Institute for Medicine has a conflict of interest policy that requires course faculty to disclose any real or apparent commercial financial affiliations related to the content of their presentations/materials. It is not assumed that these financial interests or affiliations will have an adverse impact on faculty presentations; they are simply noted in this supplement to fully inform participants. *Faculty disclosure information can be found on page 24.*



Editor's Note

Perceptions of treatment trade-offs in patients with prostate and breast cancer

Mark Soloway and I have had a friendly argument for more than a year. The root of this disagreement stems from our differences in opinion concerning prostate cancer patients' perceptions of the risk of recurrence and interventions to reduce that threat.

My hypothesis — based on a broad oncology experience, particularly in breast cancer — is that cancer patients want as much information as possible about their risk of recurrence and the potential options to increase their likelihood of remaining cancer-free. Like all experienced clinicians, Mark tailors his approach to the individual patient, but his overall impression is that “men with prostate cancer are very different from women with breast cancer.”

Even Mark's wife, Cindy — who is working on a postdoctoral thesis about the effect of prostate cancer on couples — tells me that, unlike proactive breast cancer patients, men with prostate cancer “just want to get on with their lives after radical prostatectomy and don't want to hear about further treatment.” Peter Scardino made a similar point during his interview for this program. With due respect to these experienced clinicians and others interviewed for our audio series, I wanted to find out more about the mindset of the prostate cancer patient and his spouse/partner.

To this end, Mark and I organized a “Prostate Cancer Town Meeting,” held on September 22, 2002. We spent the day with 157 prostate cancer patients, 127 spouses/partners and 26 physicians from South Florida. In front of our audience, I played the role of a patient surrogate and closely questioned Mark about the risks and benefits of various interventions. With electronic keypad polling, we queried the audience about their experiences, perceptions and the advice they would give to a friend or family member, based on a variety of clinical scenarios.

The most striking overall impression Mark and I acquired, was the dramatic heterogeneity in prostate cancer patients' experiences with the disease and perspectives on the trade-offs of various interventions. Select examples of the data collected are presented below.

Clearly, our town meeting did not provide definitive data on the complex mindset of the prostate cancer patient. However, my “argument” with Mark seems likely to continue, because our town meeting did provide me with more evidence that, while patients obviously wish to avoid treatment-related morbidity, there is an almost universal need in both men and women to take every reasonable action to avoid cancer recurrence. Why else would a man choose to have a radical prostatectomy?

On the enclosed program, I asked medical oncologist, Oliver Sartor, what his thought process would be if he were facing a 50% risk of distant progression after radical prostatectomy. He told me that he would “lean towards” androgen deprivation, but that he would assess his quality of life after a few months of treatment, and then decide whether to continue. A similar approach is common when utilizing adjuvant tamoxifen for breast cancer, and I predict that, in the future, the gap between the treatment paradigms of these two cancers will narrow considerably.

— Neil Love, MD

Prostate Cancer Town Meeting: Hollywood, Florida September 22, 2002

Select results of anonymous interactive polling of prostate cancer survivors

*How do you perceive the side-effects of the following?
(After a discussion of risks by Dr Soloway)*

A = Not a major problem.

C = Very much a problem. Only go forward if it would save my life.

B = Somewhat of a problem. Avoid if possible.

D = Extreme problem. I would not be treated with it.

	A	B	C	D
Radical prostatectomy	16%	22%	48%	14%
External beam radiation	24%	34%	33%	9%
Interstitial seed implants	36%	43%	15%	6%
LHRH agonist	18%	24%	40%	18%
Bicalutamide monotherapy	37%	37%	19%	7%
Chemotherapy	1%	11%	64%	24%

Risk of recurrence — adjuvant hormonal therapy (AHT)

- After initial therapy, 69% of the patients were not given information on their risk of recurrence.
- 93% of the patients would have liked their doctors to discuss their risk of recurrence.
- 49% of the patients and 68% of the spouses thought that doctors — particularly in high-risk situations — should present adjuvant hormonal therapy as an option.

*Would you recommend AHT to a friend with the following risk of recurrence?
(After listening to Dr Soloway discuss the risks and benefits of AHT)*

WOULD RECOMMEND AHT

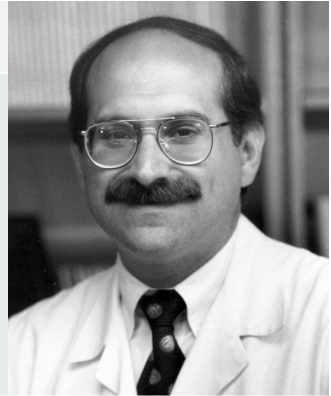
85% risk of recurrence		91%
50% risk of recurrence		41%
25% risk of recurrence		28%

Leonard G Gomella, MD, FACS

Associate Professor,
Department of Urology,
Jefferson Medical College

Director of Urologic Oncology,
Kimmel Cancer Center

Urology Chairman,
Radiation Therapy Oncology Group (RTOG)



Edited comments by Dr Gomella

CASE 1:

58-year-old man presenting with a neck mass and PSA over 500

History

In 1991, this man noticed a kiwi-sized mass in his neck while shaving. He went to the doctor, and his PSA exceeded 500 ng/ml. Biopsy of a left supraclavicular lymph node revealed metastatic adenocarcinoma, consistent with prostate cancer. The prostate was nodular on physical exam, and biopsy showed Gleason 8/9 prostate cancer throughout the gland. Abdominal CAT scan and bone scan were negative.

Follow-up

At that time, we were participating in a trial led by Paul Schellhammer evaluating combined androgen blockade — a prospective double-blind trial randomizing patients to either bicalutamide (50 mg) or flutamide combined with either goserelin or leuprolide. We entered this patient in the trial, and his PSA subsequently became undetectable. His neck mass completely disappeared, he felt fine, had no evidence of metastases and continued in the study. His PSA remained undetectable for almost eight years.

We later found out that he had been randomized to goserelin and bicalutamide, which was continued even after the trial was over. In 1999, his PSA started to bump up. It went to .5, then to 1, and then to 1.5.

We stopped the bicalutamide, and his PSA gradually came back down again. To this day, almost two years since the bicalutamide withdrawal, this man is in remission with an undetectable PSA on goserelin alone.

CASE 1 (Continued)

Case discussion

We would not have expected this man to live this long, yet he is doing very well. His PSA did not drop precipitously when we stopped the bicalutamide, but it gradually came down almost the same way it went up. We reported this case in the literature as one of the earliest cases of bicalutamide withdrawal. Interestingly, it was a durable response that has now lasted several years.

We know surprisingly little about the mechanism of antiandrogen withdrawal. Flutamide withdrawal has potentially been traced to a specific genetic alteration in the androgen receptor, causing flutamide to act as a receptor agonist, rather than a receptor blocker. The mechanism of bicalutamide withdrawal is not understood, but the withdrawal phenomenon has now been seen with all of the antiandrogens.

Most patients, however, do not have a durable response to antiandrogen withdrawal — it usually only lasts six to eight months. You can rotate antiandrogens with some patients and obtain some long-term PSA responses, putting them on and taking them off flutamide, bicalutamide or nilutamide. The medical oncologist at our center uses high-dose bicalutamide before committing to chemotherapy in patients who continue to progress after several antiandrogens.

If and when this man progresses again, we will probably try a different antiandrogen. But currently, he is stable.

El-Gabry EA, Strup SE, Gomella LG. **Undetectable prostate-specific antigen response with bicalutamide withdrawal phenomenon.** *Tech Urol* 2000;6(3):221-2. [Abstract](#)

Is combined androgen blockade more effective than castration?

Cochrane Collaborative Review Group on Prostate Diseases
Analysis of 20 major randomized trials with 6,320 patients

Conclusion:

“We find that there is a 5% improvement in the percentage of men surviving at 5 years (30% vs 25%) with combined androgen blockade with nonsteroidal antiandrogens as well as improvements in progression-free survival at 1 year. Appropriate patients with metastatic prostate cancer should be informed of the potential benefits, toxicities, and out-of-pocket expenditures.”

EXCERPT FROM: Schmitt B et al. **Combined androgen blockade with nonsteroidal antiandrogens for advanced prostate cancer: A systematic review.** *Urology* 2001;57(4):727-32. [Abstract](#)

Prostate Cancer Journal Club

Feasibility Study: Watchful waiting for localized low- to intermediate-grade prostate carcinoma with selective delayed intervention based on prostate specific antigen, histological and/or clinical progression

Choo R et al. *J Urol* 2002;167:1664-69. [Abstract](#)

The benefit of treating low- and intermediate-risk patients with observation alone is uncertain. Unfortunately, no randomized clinical trial data exist to support this approach. This paper reports a prospective cohort study of watchful waiting in patients with favorable clinical parameters — stage T1b to T2b N0M0 disease, Gleason's score of 7 or less and PSA 15 ng/ml or less.

Patients were followed with PSAs, digital rectal exams and periodic imaging studies every three months for the first two years, and every six months thereafter. They also underwent repeat biopsy 18 months after randomization.

Patients were considered to have progressed based on histological change on repeat biopsy, physical change in the digital rectal exam, or a change in symptoms. The investigators also looked at the PSA-doubling times.

Results are reported in 206 patients with a mean follow-up time of 29 months. About two-thirds (137) remained on the surveillance protocol with no evidence of disease progression, while the other third (69) were withdrawn for various reasons — clinical progression, PSA progression, higher Gleason scores on repeat biopsy, death from other causes, and request to be treated more actively.

The estimated actuarial probability of remaining on the surveillance protocol was 67 percent at two years and 48 percent at four years. The probability of a patient remaining progression-free was 81 percent at two years and 67 percent at four years.

This paper begins to give us parameters to follow patients with low- to intermediate-risk prostate cancer. In addition, as reported in this study, patients may then receive treatment upon clinical, PSA or histological progression, without adverse effects on outcome.

We do not have any prospective, observational, longitudinal trial information specifically looking at observation in patients with prostate cancer. This is one of the first papers to begin to define parameters for this strategy.

In an editorial comment, Dr. Peter Albertsen, from the University of Connecticut, notes that this will be an important paper to begin to establish how patients may be followed optimally by observation.

*Prospective evaluation of prostate cancer detected on biopsies 1, 2, 3 and 4:
When should we stop?*

Djavan B et al. *J Urol* 2001;166:1679-83. [Abstract](#)

This prospective trial evaluated 1,051 men with PSAs between four and ten. The authors evaluated biochemical parameters, pathologic features and biopsy-related morbidity on a series of four transrectal biopsies.

If the first biopsy was negative, patients had a second biopsy six weeks later. If the second biopsy was negative, they had a third biopsy eight weeks later. If the third was negative, biopsy four was performed eight weeks later.

Patients in the study had more complications with biopsies three and four than with biopsies one and two. In addition, the cancers discovered on biopsies three and four tended to have very favorable characteristics — low Gleason scores and organ-confined disease.

These results suggest that the yield after two negative sextant biopsies is fairly low in men with mildly elevated screening PSA. The authors concluded that without a high suspicion of cancer and/or poor prognostic factors on first or second biopsy, the third and fourth biopsies do not usually yield much additional information. According to this study, if the PSA rises again, you can do another biopsy, and any cancer found is likely to be a very favorable cancer.

This study used a very aggressive biopsy schema — performing biopsies every six to eight weeks. In the United States, most people wait three to six months after a negative biopsy before repeating it.

I generally just follow most men with two completely negative biopsies within a three- to six-month period. This study gives me more confidence in that approach. These results should help ease the minds of patients with elevated but stable PSAs.

Authors' conclusions

"Prostate cancer on biopsy 2 is not an uncommon finding and will be encountered in 10% of cases. In contrast, cancer detection on biopsies 3 (5%) and 4 (4%) is rare. Despite differences in location and multifocality, pathological and biochemical features of cancer detected on biopsies 1 and 2 were similar, suggesting comparable biological behaviors. However, cancer detected on biopsies 3 and 4 had a lower grade, stage and volume compared with biopsies 1 and 2. Therefore, biopsy 2 in all cases of a negative finding on biopsy 1 appears justified. However, biopsies 3 and 4 should only be obtained in select patients with a high suspicion of cancer and/or poor prognostic factors on biopsy 1 or 2."

EXCERPT FROM: Djavan B et al. *J Urol* 2001;166:1679-83. [Abstract](#)

Select publications

Carter HB et al. Expectant management of nonpalpable prostate cancer with curative intent: Preliminary results. *J Urol* 2002;167(3):1231-4. [Abstract](#)

Djavan B et al. Repeat prostate biopsy: Who, how and when? A review. *Eur Urol* 2002;42(2):93. [Abstract](#)

Djavan B et al. Safety and morbidity of first and repeat transrectal ultrasound guided prostate needle biopsies: Results of a prospective European prostate cancer detection study. *J Urol* 2001;166(3):856-60. [Abstract](#)

El-Gabry EA et al. Undetectable prostate-specific antigen response with bicalutamide withdrawal phenomenon. *Tech Urol* 2000;6(3):221-2. [Abstract](#)

Errejon A, Crawford ED. Monotherapy versus combined androgen blockade in patients with advanced prostate cancer. *Cancer* 2002;95(2):209-10. [Abstract](#)

Huan SD et al. Antiandrogen withdrawal syndrome with nilutamide. *Urology* 1997;49(4):632-4. [Abstract](#)

Klotz LH et al. Expectant management with selective delayed intervention for favorable-risk prostate cancer. *Can J Urol* 2002;9(3 Supp 1):2-7. [Abstract](#)

Nieh PT. Withdrawal phenomenon with the antiandrogen casodex. *J Urol* 1995;153(3 Pt 2):1070-2;discussion 1072-3. [Abstract](#)

Paul R, Breul J. Antiandrogen withdrawal syndrome associated with prostate cancer therapies: Incidence and clinical significance. *Drug Saf* 2000;23(5):381-90. [Abstract](#)

Roehl KA et al. Serial biopsy results in prostate cancer screening study. *J Urol* 2002;167(6):2435-9. [Abstract](#)

Samson DJ et al. Systematic review and meta-analysis of monotherapy compared with combined androgen blockade for patients with advanced prostate carcinoma. *Cancer* 2002;95(2):361-76. [Abstract](#)

Schellhammer PF et al. Prostate specific antigen decreases after withdrawal of antiandrogen therapy with bicalutamide or flutamide in patients receiving combined androgen blockade. *J Urol* 1997;157(5):1731-5. [Abstract](#)

Schellhammer PF, Kolvenbag GJ. Serum PSA decline after Casodex withdrawal. *Urology* 1994;44(5):790-2. [Abstract](#)

Stephenson AJ et al. Utility of PSA doubling time in follow-up of untreated patients with localized prostate cancer. *Urology* 2002;59(5):652-6. [Abstract](#)

Zietman AL et al. Conservative management of prostate cancer in the prostate specific antigen era: The incidence and time course of subsequent therapy. *J Urol* 2001;166(5):1702-6. [Abstract](#)

Peter R Carroll, MD

Professor and Chair,
Department of Urology,
University of California, San Francisco

Program Leader,
Program in Urologic Oncology,
Mt Zion Cancer Center,
University of California, San Francisco

Interim Chief of Urology,
Mt Zion Medical Center,
University of California, San Francisco



Edited comments by Dr Carroll

Cancer of the Prostate Strategic Urologic Research Endeavor (CaPSURE)

CaPSURE is an observational registry being conducted at about 35 sites — mainly community physicians' offices — around the United States. Consecutive patients with prostate cancer of all ages, stages and treatment modalities are enrolled. The objective is to evaluate prostate cancer treatment trends and outcomes.

I believe that CaPSURE is providing a representative picture of prostate cancer care in the United States. When we compare the outcomes in CaPSURE to those at academic medical centers, they are reasonably close. We see a stage migration — lower stage disease, lower median PSA, younger patients with more favorable disease.

Prostate cancer treatment patterns

We are detecting rather remarkable changes in treatment patterns, over time. Currently, 30% to 40% of men are still treated with radical prostatectomy. Another 30% may receive radiation therapy alone or in combination with hormonal therapy. The rest are either observed or treated with hormonal therapy.

There are many more men with low-risk prostate cancer now being managed with brachytherapy and fewer with radical prostatectomy. The number of patients being observed is relatively stable — about eight percent. Men with intermediate-risk prostate cancer are being treated with radiation therapy and radical prostatectomy. In men with high-risk prostate cancer, more hormonal therapy is being prescribed.

CaPSURE has noted two other treatment trends — more neoadjuvant hormonal therapy in combination with radiation therapy, and the use of hormonal therapy as primary therapy in men with nonmetastatic disease in all risk groups. This trend is greater in patients with high-risk (high grade or volume) disease.

Currently, in the United States we are not seeing the use of antiandrogens as primary therapy very frequently. However, I think that this is going to change, and we will see more bicalutamide given as primary therapy. My sense is that bicalutamide monotherapy will be used in patients with high-risk (high grade and volume) localized disease (M0), who do not want or are not candidates for standard therapy.

CaPSURE database: Use of primary androgen deprivation therapy (ADT) in 1,485 consecutive prostate cancer cases

ADT Alone (294)		20%
Neoadjuvant ADT+RP (184)		12%
Neoadjuvant ADT+RT (116)		8%

RP = radical prostatectomy, RT = radiation therapy

DERIVED FROM: Meng MV et al. Contemporary patterns of androgen deprivation use for newly diagnosed prostate cancer. *Urology* 2002;60(suppl 3A):7-12. [Abstract](#)

Primary hormonal therapy for prostate cancer

Increasingly, older men with comorbidities and high-risk, nonmetastatic prostate cancer are initially being treated with hormonal therapy — an intermittent LHRH agonist or bicalutamide monotherapy. The effect of hormonal therapy on the primary tumor is more durable than on metastatic disease.

In a patient with an estimated survival of five years or less, based on age and comorbidity, aggressive local therapy will not make a difference. We can control prostate cancer well with systemic therapy, certainly in the three- to five-year range, in patients with low- or intermediate-risk disease and even high-risk, nonmetastatic disease.

For patients with M0 disease, data suggest that bicalutamide 150 mg and an LHRH agonist are both reasonable options. Bicalutamide seems to preserve health-related quality of life, sexual function and bone mineral density compared to an LHRH agonist.

Management of patients with biochemical relapse

This is the largest group currently receiving hormonal therapy. First, biochemical progression must be confirmed with another PSA, and it is also important to get a sense of the PSA kinetics — the rate and timing of rise. The primary disease characteristics should also be considered. Those two factors — more than imaging — allow you to determine the approach to treatment.

The typical patient with a local recurrence has Gleason 7 or less with a late failure (after two years), PSA doubling time more than 10 months, and no seminal vesicle invasion or positive nodes. The typical patient with systemic recurrence has Gleason 8 to 10 prostate cancer, PSA greater than 20 and early failure (before two years).

There may be a tendency in some physicians to ignore the importance of biochemical recurrence, but one should have an honest discussion with the patient about the treatment options and trade-offs.

These patients are candidates for either clinical trials or systemic therapy. Outside of a clinical trial, patients failing systemically are candidates for hormonal therapy — an LHRH agonist (continuous or intermittent) or bicalutamide. One needs to have a careful discussion with the patient about what they can expect from one form of treatment or another.

Bicalutamide 150 mg is a reasonable treatment option for the patient who wants to maintain sexual function and understands the risk of gynecomastia. Most men do not find gynecomastia a real issue. For men who are physically or sexually active, declines in physical and sexual function seen with LHRH agonists may be a bigger trade-off.

Management of patients with high-risk prostate cancer

I consider combination therapy in patients with a high probability of failing local therapy. One option is surgery followed by adjuvant radiation or systemic therapy. Another option is neoadjuvant hormonal therapy followed by 3-D conformal radiation therapy to the prostate and regional lymph nodes.

Currently, we have a trial comparing chemo/hormonal therapy to hormonal therapy alone in patients with node-positive disease. However, the most common type of treatment for this situation is hormonal therapy — either bicalutamide 150 mg or an LHRH agonist.

When discussing hormonal therapy with these patients, I tell them that early therapy may delay progression and provide a survival benefit, but we do not know how early is early. Most patients will delay hormonal therapy and monitor their PSA.

CASE 2:

49-year-old man with Gleason 4+3 prostate cancer

History

The patient was recently divorced, in a new relationship and ignoring a prostate cancer diagnosis. His parents came for a consultation with me and audio taped it for him. Ultimately, another urologist on the East Coast and I evaluated the patient.

There was no family history of prostate cancer. His PSA was 16 ng/mL, and he had 90% of the cores involved with Gleason 4+3 prostate cancer. His bone scan was negative. He clearly had locally advanced disease on palpation, and we demonstrated by ultrasound that there was invasion at the base of the seminal vesicles. His quality of life and sexual function were good.

Follow-up

He is currently undergoing hormonal therapy with an LHRH agonist. He will also receive bicalutamide, for at least one month. A radiation oncologist has evaluated him for 3-D conformal radiation therapy.

Case discussion

TREATMENT OPTIONS:

Based on his PSA, Gleason score and the number of positive biopsies, he was considered a high-risk patient. I thought the likelihood of this patient being cured with radical prostatectomy was quite low. He was not a good candidate for monotherapy and required combination therapy. His choices were either surgery with a node dissection followed by adjuvant therapy, or neoadjuvant hormonal therapy and radiation to the prostate and pelvis.

He elected neoadjuvant hormonal therapy and radiation therapy. Despite his high risk of nodal involvement, a lymph node dissection was not necessary. We were going to treat him with the full-field radiation, whether or not the nodes were involved.

In terms of hormonal therapy options, he was offered an LHRH agonist or bicalutamide monotherapy. I told him, "We have the most information with the LHRH agonists, and the decision to use an LHRH agonist is not permanent. We can start out with a one-month injection, and we can change forms of hormonal treatment in the future." Even though bicalutamide monotherapy might not interfere as much with sexual function and quality of life, he decided to receive an LHRH agonist.

In patients who are strongly averse to an LHRH agonist, I switch them from an LHRH agonist to bicalutamide monotherapy, just to keep them on some form of hormonal therapy. In this patient, I would use an LHRH agonist, evaluate his response and tolerability, and then make a decision about bicalutamide later.

The timing and duration of hormonal therapy is negotiable. Normally, for high-risk patients, we treat for two years. In this situation, because of PSA monitoring, there is the opportunity to, perhaps, treat him for a shorter period of time and then restart. We have negotiated with this patient to start an LHRH agonist and monitor his PSA, tumor volume and tolerability of therapy.

CASE 2 (Continued)

My sense is that he should be on hormonal therapy for at least 8 to 12 months, and after that, it might be negotiable. If he tolerates therapy well, I think he should continue. If his quality of life is impaired, then maybe we will stop it, follow his PSA kinetics and consider treatment if his PSA rises in the future.

PSYCHOSOCIAL ISSUES:

For young patients, prostate cancer is not on their radar screen, and the overwhelming concern in this man's life is death from prostate cancer. He was consumed with the idea that he would die shortly and that he had no future. He is at high risk, but I told him that I felt very confident that he was going to have a response — that the PSA was going to go down, tumor volume would go down — and that radiation and hormonal therapy was going to affect his cancer favorably. Men in this situation need to understand that, and that at the same time, we're working hard through research to look at novel treatment strategies.

At this point, I think he's coping very well. This is also a situation where you want to make a solid commitment that you're going to be there not only now, but that you have a treatment plan in place for later if current treatment therapy fails.

His significant other is very supportive, and her expression of that support was very important to him. Most significant others are more risk-averse than the patient themselves and want more aggressive treatment than the actual patient. They want to leave no stone unturned for cure, even though they understand that might impact quality of life.

Impact of psychosocial intervention to improve coping skills

We have an ongoing randomized trial evaluating the role of psychosocial intervention to improve coping skills in patients with prostate cancer. Patients are randomized to receive psychosocial intervention focusing on coping skills with a psychologist, or to receive no intervention.

The primary endpoints are health-related quality of life, emotional well-being and fear of cancer recurrence. Secondly, we will look at differences in PSA outcomes, but that will not be evaluated for many years. It may be that psychosocial intervention correlates with other things, such as how people seek additional treatment.

Prostate cancer management strategies

I think there is going to be a great paradigm shift in two areas of prostate cancer, relatively soon. First, there are some patients who are being overtreated. This is supported by two recent clinical trials and data from CaPSURE.

Certain older patients with comorbidities and low-stage, low-volume and low-grade prostate cancer may be watched and treated selectively based on parameters of progression — PSA change or selective biopsy at 24 months. At UCSF, we are conducting clinical trials to evaluate initial surveillance and selective therapy for low-risk patient populations.

On the other hand, we may not have been aggressive enough in high-risk patients. So, we will assess combination and novel therapies in those patients. In one patient population we will treat less aggressively, and for patients with intermediate- and high-risk prostate cancer, we will treat more aggressively.

Select publications

Cooperberg MR et al. Contemporary trends in imaging test utilization for prostate cancer staging: Data from the Cancer of the Prostate Strategic Urologic Research Endeavor. *J Urol* 2002;168:491-5. [Abstract](#)

Grossfeld GD et al. Patterns of failure after primary local therapy for prostate cancer and rationale for second therapy. *Urology* 2002;60(Suppl 3A):57-62. [Abstract](#)

Grossfeld GD et al. Predicting disease recurrence in intermediate- and high-risk patients undergoing radical prostatectomy using percent positive biopsies: Results from CaPSURE. *Urology* 2002;59:560-5. [Abstract](#)

Grossfeld GD et al. Predictors of secondary cancer treatment in patients receiving local therapy for prostate cancer: Data from CaPSURE. *J Urol* 2002;168:530-5. [Abstract](#)

Grossfeld GD et al. Under staging and under grading in a contemporary series of patients undergoing radical prostatectomy: Results from CaPSURE. *J Urol* 2001;165:851-6. [Abstract](#)

Litwin MS et al. Mental health in men treated for early stage prostate cancer: A post-treatment, longitudinal, quality of life analysis from CaPSURE. *Cancer* 2002;95(1):54-60. [Abstract](#)

Litwin MS et al. Quality of life before death for men with prostate cancer: Results from CaPSURE. *J Urol* 2001;165:871-5. [Abstract](#)

Lubeck DP et al. Health related quality of life differences between black and white men with prostate cancer: Results from CaPSURE. *J Urol* 2001;166:2281-5. [Abstract](#)

Meng MV et al. Contemporary patterns of androgen deprivation use for newly diagnosed prostate cancer. *Urology* 2002;60(Suppl 3A):7-11. [Abstract](#)

Moul J et al. Predicting risk of prostate specific antigen recurrence after radical prostatectomy with the Center for Prostate Disease Research and Cancer of the Prostate Strategic Urologic Research Endeavor databases. *J Urol* 2001;166:1322-7. [Abstract](#)

Penson DF et al. How well does the Partin nomogram predict pathological stage after radical prostatectomy in a community-based population? Results from CaPSURE. *J Urol* 2002;167:1653-8. [Abstract](#)

Penson DF et al. Relationship of first-year costs of treating localized prostate cancer to initial choice of therapy and stage at diagnosis: Results from CaPSURE. *Urology* 2001;57(3):499-503. [Abstract](#)

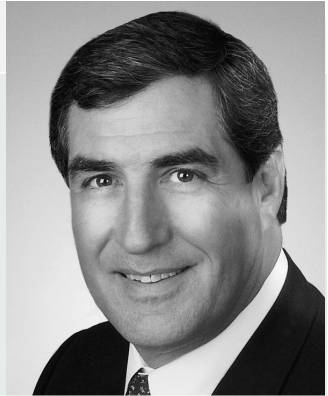
Penson DF et al. The association between socioeconomic status, health insurance coverage and quality of life in men with prostate cancer. *J of Clinical Epidemiology* 2001;54(4):350-8. [Abstract](#)

Peter T Scardino, MD

Chairman, Department of Urology;
Head, Prostate Cancer Program,
Memorial Sloan-Kettering Cancer Center

Professor of Urology,
Weill Medical College,
Cornell University

Professor of Urology,
SUNY Downstate Medical School



Edited comments by Dr Scardino

Multimodality approach to prostate cancer

We have learned from testicular, breast and colorectal cancer that, even with superb local therapy, multimodality treatment in some patients is the key to cure. Therefore, it is important that we do more studies in prostate cancer and look at this issue, carefully.

Looking back at urology over the last 25 or 30 years, the attitude has been that hormonal therapy does not cure prostate cancer or prolong survival. That attitude has led many in the urology community to be skeptical about the value of adjuvant systemic hormonal therapy trials and to argue that, not only should patients not be treated, but also that the trials should not even be done. I think that this is a mistake.

If we can find evidence that adjuvant hormonal therapy really adds to the benefit of optimal local treatment, we should learn about it and apply it, as soon as possible. I am impressed with the bicalutamide randomized trial data, and we need to determine if there is a survival benefit. If a trial demonstrates reduced mortality associated with adjuvant hormonal therapy, I think this approach will be widely adopted.

Patients' wishes to avoid postsurgical radiation therapy

Although its impact on survival and clinical progression is not known, there is good evidence that radiation therapy can reduce the risk of PSA recurrence in men with positive margins. The downsides to radiation therapy include inconvenience, cost, a very small risk of worse urinary control, and a significant risk of interfering with the recovery of erectile function. In my experience, with this risk-benefit assessment, only one out of five men will elect radiation therapy for positive margins.

Decision-making process about adjuvant hormonal therapy

The key questions patients should have answers to when decision-making are: What risk does this tumor pose to me? How likely am I to have a positive bone scan? How likely am I to develop symptoms from the tumor? How likely am I to die from this cancer? What price do I pay by taking these drugs? Different men will make different decisions with this input.

If a therapy demonstrated a 30% reduction in mortality, I think the overwhelming majority of patients would accept side-effects and elect to receive treatment. Until we have survival data, the decision is more of a trade-off. Our job is to give patients the best possible information so that they can make an informed decision about the risks and benefits of therapy.

Prostate cancer patients have an excellent early-warning system that is almost foolproof, and it is rare for a patient to develop a recurrence without a rising PSA. Patients may say, "This is a good decision, but the right time for me to make it is when my PSA rises. If I am lucky enough to be in the group whose PSA never rises, I have safely avoided it. If I am in the group whose PSA rises, I still have plenty of time to obtain the benefit from early hormonal therapy."

Endocrine therapy in men with positive lymph nodes

The choice here is either to begin hormonal therapy after surgery, or to wait and see what happens with the PSA. Although there have been randomized trials suggesting prolonged survival for men treated with early rather than late hormonal therapy, we really do not know how early is early. I think we probably have plenty of time if patients decide to wait until their PSA rises, but I do not know exactly.

I explain the following to patients: "If we give you hormonal therapy now, it will prolong the time until your PSA rises and your cancer comes back, but I do not know if it will prolong your life." A small study by Messing suggests it does, but there are some problems with that study because patients either received hormonal therapy immediately, or when the disease came back, clinically. Today with PSA monitoring, we can start treatment somewhere between those two points and still treat earlier. The advantage to waiting would be two and a half years, on average, before starting hormonal therapy. The disadvantages may be earlier progression or decreased survival, but we do not know that. Given that discussion, about half of patients would not want any treatment and would elect to watch their PSA while the other half would elect adjuvant hormonal therapy.

We use nomograms to try to judge the risk of recurrence in patients. Anytime the risk of recurrence is above 20%, I feel an obligation to carefully inform the patient about what the recurrence might mean, the options for treatment and when the treatment can be introduced.

Selection of hormonal therapy

Our classic hormonal therapy has been castration. Since the publication of the Early Prostate Cancer (EPC) data, bicalutamide now seems like a valid approach. Probably in the future, bicalutamide will become a more common form of hormonal therapy for men electing hormonal therapy.

When discussing hormonal therapy, I tell patients: “You can either have your testicles removed or you can receive an injection every month or every three months. At the beginning, we sometimes combine the injection with a pill that blocks the side-effects from the injection. You can also just take a pill. The options are thought to have the same effect on the tumor.

The differences are a matter of convenience — taking a pill compared to receiving a shot. There may be some cost differences, depending upon what your insurance covers. The daily pill is more likely than the shot to cause problems with breast swelling or tenderness. But the pill may be less likely to interfere with libido or recovery of your erections.”

Of the men electing adjuvant hormonal therapy, the majority elects castration and few choose an antiandrogen. But, I think that is because the data with the antiandrogens is relatively new. We are in a changing phase, and my guess is that, in the future, this will probably reverse, and many men will select antiandrogen therapy because of the decreased risk of impotence. Those men will be willing to accept an increased risk of gynecomastia and breast pain for a decreased risk of a diminished libido and impotence.

Antiandrogen monotherapy

Although there may be a little debate, I think there is enough data to say antiandrogen monotherapy is probably equivalent to castration in terms of cancer control. The attraction has been less of an impact on libido and erectile function with bicalutamide than castration.

Today, the antiandrogen regimen of choice is bicalutamide 150 mg. We have always considered it when sexual function was an important issue for the patient. Even 10 or 15 years ago, I was treating those patients concerned about their sexual function and not wanting medical or surgical castration with flutamide alone for positive nodes or an early rising PSA. In patients with sexual function, I have always considered antiandrogens for biochemical or clinical progression and in the adjuvant setting.

It has been the uncommon choice in the past. But I think that with the newer data on bicalutamide’s long-term use in the adjuvant setting, antiandrogen monotherapy will be used more in the future.

Select publications

Bolla M et al. **Improved survival in patients with locally advanced prostate cancer treated with radiotherapy and goserelin.** *N Engl J Med* 1997;337:295-300. [Abstract](#)

Bolla M et al. **Long-term results with immediate androgen suppression and external irradiation in patients with locally advanced prostate cancer (an EORTC study): A phase III randomised trial.** *Lancet* 2002;360(9327):103-6. [Abstract](#)

Catton C et al. **Adjuvant and salvage radiation therapy after radical prostatectomy for adenocarcinoma of the prostate.** *Radiother Oncol* 2001;59(1):51-60. [Abstract](#)

Do LV et al. **Postoperative radiotherapy for carcinoma of the prostate: Impact on both local control and distant disease-free survival.** *Am J Clin Oncol* 2002;25(1):1-8. [Abstract](#)

Grossfeld GD et al. **Management of a positive surgical margin after radical prostatectomy: Decision analysis.** *J Uro* 2000;164(1):93-9. [Abstract](#)

Iversen P et al. **Bicalutamide monotherapy compared with castration in patients with nonmetastatic locally advanced prostate cancer: 6.3 years of follow-up.** *J Urol* 2000;164:1579-82. [Abstract](#)

The Medical Research Council Prostate Cancer Working Party Investigator Group. **Immediate versus deferred treatment for advanced prostatic cancer: Initial results of the Medical Research Council trial.** *Br J Urol* 1997;79:235-46. [Abstract](#)

Messing EM et al. **Immediate hormonal therapy compared with observation after radical prostatectomy and pelvic lymphadenectomy in men with node-positive prostate cancer.** *New Engl J Med* 1999;341:1781-8. [Abstract](#)

Oosterlinck W et al. **Tolerability and safety of flutamide in monotherapy, with orchiectomy or with LHRHa in advanced prostate cancer patients. A Belgian multicenter study of 905 patients.** *Eur Urol* 1996;30(4):458-63. [Abstract](#)

Schroder FH et al. **Prostate cancer treated by antiandrogens: Is sexual function preserved? EORTC Genitourinary Group. European Organization for Research and Treatment of Cancer.** *Br J Cancer* 2000;82(2):283-90. [Abstract](#)

See WA et al. **Bicalutamide as immediate therapy either alone or as adjuvant to standard care of patients with localized or locally advanced prostate cancer: First analysis of the early prostate cancer program.** *J Urol* 2002;168(2):429-35. [Abstract](#)

Tyrrell CJ et al. **A randomised comparison of 'Casodex' (bicalutamide) 150 mg monotherapy versus castration in the treatment of metastatic and locally advanced prostate cancer.** *Eur Urol* 1998;33(5):447-56. [Abstract](#)

A Oliver Sartor, BA, MD

Director, Stanley S Scott Cancer Center

Chief, Hematology/Oncology;
Professor of Medicine and Urology,
Louisiana State University Health Sciences
Center

Ad Hoc Member, US FDA Administration,
Medical Imaging and Device Advisory
Committee (MIDAC)



Edited comments by Dr Sartor

Prostate Cancer Journal Club

Extended pelvic lymphadenectomy in patients undergoing radical prostatectomy: High incidence of lymph node metastasis

Heidenreich A et al. *J Urol* 2002;167(4):1681-6. [Abstract](#)

The definition of advanced disease in prostate cancer has changed over the last decade. Today, a diagnosis of Stage D-1 disease has very clear therapeutic implications, because the data from Messing and colleagues show a survival benefit for treating patients with Stage D-1 disease with early or immediate hormonal therapy. Therefore, accurate staging is critical.

This study, in the *Journal of Urology*, demonstrates that patients receiving standard lymphadenectomy are probably being understaged and physicians may be missing opportunities for early treatment.

Currently, standard lymph node dissection during radical prostatectomy includes the external iliac and obturator nodes, with an average yield of ten lymph nodes. This paper compares 100 patients undergoing standard lymphadenectomy to 103 patients undergoing extended lymphadenectomy in which the internal iliacs, common iliacs and presacrals are also dissected. The two patient series were very similar with regard to Gleason scores, PSAs and patients' ages.

The results showed a doubling in the incidence of node-positive disease in the extended lymphadenectomy group. Only 12% of the patients had node-positive disease in the standard dissection group, whereas 26% had node-positive disease in the extended dissection group. The toxicities were essentially the same with no excess morbidity in the extended dissection group.

Careful cataloging of the location of the lymph node metastases revealed that 42% in the extended procedure were outside of the regions of the standard pelvic lymphadenectomy. There were at least six patients who had internal iliac metastases that would have been missed if this area had not been dissected. Researchers found no value in presacral dissection. Only one patient had presacral involvement, and that patient had involvement in other areas as well. They concluded that pelvic lymphadenectomy should include dissection of the internal iliac, external iliac and obturators fossa groups.

This paper is also interesting as it relates to a variety of studies with the ProstaScint Monoclonal Antibody Scan. Patients who had a positive scan and a negative dissection were classified as “false positives.” The findings of this article suggest that the standard lymph node dissection may be inadequate for proper staging.

Improved staging methods are needed to ensure staging accuracy. Until we know the extent of the patient’s disease, we will continue to subject patients to treatments that may fail.

Osteoporosis in men treated with androgen deprivation therapy for prostate cancer

Ross RW, Small EJ. *J Urol* 2002 May;167(5):1952-6. **Abstract**

This review paper notes that androgen deprivation leads to an increased risk of osteoporosis, and discusses the implications of this as we subject men to androgen deprivation earlier in the treatment of prostate cancer.

Bone mineral density peaks relatively early in life and bone loss begins at about age 30. In quantifying bone loss over time, one can then expect about a one percent bone mineral density loss per year. Androgen deprivation increases that loss to about four percent during the first couple of years and then it drops to two percent around years three and four.

Clearly, bone loss becomes more serious as the duration of deprivation increases. If we treat younger men earlier, they may be living with androgen deprivation for decades.

This raises several interesting questions: How much osteopenia and osteoporosis has a clinically meaningful endpoint? What is a reliable laboratory measurement? What translates into a fracture rate? The author cites four different studies, and the percentage of osteoporotic fracture varies from four to 50 percent — a wide variance. Part of the variance is due to a variation in follow-up. In addition, the analyses were predominantly retrospective. It is fairly clear that if you follow people for a period of time, the fracture rate goes up as a function of time.

One of the important points made in this article is that, if we are going to treat patients with hormonal therapy, particularly in clinical trials, we need to improve our monitoring of osteoporosis and fracture rates.

Other interesting questions are, how often should you measure bone loss, and

when should you intervene? Men start with a higher bone mass density than women, so men can lose more bone mass, and it may not be clinically relevant. There are very poor data with regards to how much bone mass men need to lose before the osteoporotic risk increases. This article recommends a baseline measurement before androgen deprivation therapy begins, and another one year later. Other than exercise, calcium and Vitamin D, which are all relatively benign, it is not clear whether or not we should use other aggressive interventions.

There are data that show bisphosphonates can either diminish bone loss or actually restore bone. Analogous to the breast cancer literature with pamidronate, zoledronate has been associated with fewer skeletal-related events. Pamidronate was very equivocal in the prostate studies, but zoledronate was not. Zoledronate is now FDA-approved and commercially available for patients with hormone-refractory disease and skeletal metastases. While some people advocate treating patients with prophylactic bisphosphonates, I think we need more data.

In addition to the bisphosphonate question, one could question estrogen therapy. We can use estradiol, the estrogen patches or low-dose DES. The role of estrogens in treating this complication is unknown, as we do not have the data.

In summary, it is unequivocal that androgen deprivation leads to an acceleration of bone loss, and it probably increases the osteoporotic fracture rate. More data are needed, however, particularly on reversal of osteoporosis in terms of what agents to use and the timing of intervention. Vitamin D, calcium and exercise are all reasonable, and patients should be counseled about smoking and excessive alcohol use, which contribute to osteoporosis. Whether or not we treat with bisphosphonates needs to be answered in clinical trials designed with relevant end points.

Relationship between obesity and race in predicting adverse pathologic variables in patients undergoing radical prostatectomy

Amling CL et al. *Urology* 2001;58(5):723-8. **Abstract**

This paper describes a study in which 860 prostate cancer patients undergoing radical prostatectomy were categorized by body mass index into three groups: obese, overweight and normal. Each group was then compared in terms of age, race, PSA, Gleason score, and pathologic stage.

The initial uni-variant analysis showed a relationship between obesity and poor prognostic factors. Obese patients presented at a younger age, had a higher Gleason score on average, had a greater percentage of high-grade Gleason scores, and were less likely to have organ-confined disease. They also found a higher percentage of African-American patients in the obese group.

Race was an interesting finding because African-Americans present with prostate cancer at a younger age, and with higher Gleason scores. The

findings indicate that obesity may, at least in part, account for the ethnic variability related to the poorer prognostic factors. On multi-variate analysis, body mass index was the only factor that predicted the Gleason score and the stage after radical prostatectomy.

The bottom line on this study is that obesity is associated with an early onset of prostate cancer, as well as a higher Gleason score and a higher percentage of nonorgan-confined disease. Even though we already knew that we should not be obese, we now have one more reason to avoid it.

Select publications

Arai Y et al. **Incidence of lymph node metastasis and its impact on long-term prognosis in clinically localized prostate cancer.** *Int J Urol* 1998;5(5):459-65. [Abstract](#)

Bader P et al. **Is a limited lymph node dissection an adequate staging procedure for prostate cancer?** *J Urol* 2002;168(2):514-8;discussion 518. [Abstract](#)

Berruti A et al. **Changes in bone mineral density, lean body mass and fat content as measured by dual energy X-ray absorptiometry in patients with prostate cancer without apparent bone metastases given androgen deprivation therapy.** *J Urol* 2002;167(6):2361-7;discussion 2367. [Abstract](#)

Bissonette EA et al. **Prostate specific antigen kinetics at tumor recurrence after radical prostatectomy do not suggest a worse disease prognosis in black men.** *J Urol* 2001;166(4):1328-31;discussion 1331-2. [Abstract](#)

Burkhard F et al. **Reliability of preoperative values to determine the need for lymphadenectomy in patients with prostate cancer and meticulous lymph node dissection.** *Eur Urol* 2002;42(2):84. [Abstract](#)

Daniell HW. **Osteoporosis due to androgen deprivation therapy in men with prostate cancer.** *Urology* 2001;58(2 Suppl 1):101-7. [Abstract](#)

Fergany A et al. **No difference in biochemical failure rates with or without pelvic lymph node dissection during radical prostatectomy in low-risk patients.** *Urology* 2000;56(1):92-5. [Abstract](#)

Fowler JE Jr et al. **Race and cause-specific survival with prostate cancer: Influence of clinical stage, Gleason score, age and treatment.** *J Urol* 2000;163(1):137-42. [Abstract](#)

Freedland SJ et al. **Race is not an independent predictor of biochemical recurrence after radical prostatectomy in an equal access medical center.** *Urology* 2000;56(1):87-91. [Abstract](#)

Hoffman RM et al. **Racial and ethnic differences in advanced-stage prostate cancer: The Prostate Cancer Outcomes Study.** *J Natl Cancer Inst* 2001;93(5):388-95. [Abstract](#)

Kiratli BJ et al. **Progressive decrease in bone density over 10 years of androgen deprivation therapy in patients with prostate cancer.** *Urology* 2001;57(1):127-32. [Abstract](#)

Link RE, Morton RA. **Indications for pelvic lymphadenectomy in prostate cancer.** *Urol Clin North Am* 2001;28(3):491-8. [Abstract](#)

Moyad MA. **Complementary therapies for reducing the risk of osteoporosis in patients receiving luteinizing hormone-releasing hormone treatment/orchiectomy for prostate cancer: A review and assessment of the need for more research.** *Urology* 2002;59(4 Suppl 1):34-40. [Abstract](#)

Shackley DC et al. **Staging laparoscopic pelvic lymphadenectomy in prostate cancer.** *BJU Int* 1999;83(3):260-4. [Abstract](#)

Smith MR. **Osteoporosis during androgen deprivation therapy for prostate cancer.** *Urology* 2002;60(3 Suppl 1):79-85;discussion 86. [Abstract](#)

Pharmaceutical agents discussed in this program

GENERIC	TRADE	MANUFACTURER
bicalutamide	Casodex®	AstraZeneca Pharmaceuticals, LP
goserelin	Zoladex®	AstraZeneca Pharmaceuticals, LP
nilutamide	Nilandron®	Aventis Pharmaceuticals
leuprolide	Lupron®	TAP Pharmaceuticals
pamidronate	Aredia®	Novartis Pharmaceuticals
flutamide	Chimax, Drogenil®	Various manufacturers
zoledronate	Zometa®	Novartis Pharmaceuticals

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Faculty financial interests or affiliations

Leonard G Gomella, MD, FACS

Speakers' Bureau: AstraZeneca Pharmaceuticals, LP

Peter R Carroll, MD

Does not have any financial interests or affiliations to disclose.

Peter T Scardino, MD

Grants/Research Support: National Cancer Institute

Stockholder: Proquest

A Oliver Sartor, BA, MD

Stockholder: Atrix Laboratories

Speakers' Bureau: AstraZeneca Pharmaceuticals, LP; Schering-Plough Corporation

Questions *(please circle answer)*

1. There is a 5% 5-year survival benefit with combined androgen blockade (LHRH plus a nonsteroidal antiandrogen) compared to LHRH alone.
 - a. True
 - b. False
2. The mechanism of antiandrogen withdrawal is well-understood.
 - a. True
 - b. False
3. Which of the following did Choo R et al use to detect progression in prostate cancer patients offered watchful waiting?
 - a. Digital rectal exam
 - b. Repeat biopsy
 - c. PSA
 - d. Imaging studies
 - e. All of the above
4. Which of the following statements were true of the results of Djavan B et al's study of sequential prostate biopsies?
 - a. Patients had more complications with biopsies 3 and 4 than with biopsies 1 and 2.
 - b. Biopsies 3 and 4 tended to yield valuable information when biopsies 1 and 2 were negative.
 - c. Cancers discovered on biopsies 3 and 4 tended to have low Gleason's score and organ-confined disease.
 - d. a and c
 - e. all of the above
5. CaPSURE is an observational registry of prostate cancer patients treated primarily at academic medical centers.
 - a. True
 - b. False
6. CaPSURE has noted which of the following treatment trends?
 - a. More neoadjuvant hormonal therapy is being used in combination with radiation therapy among patients in all risk groups.
 - b. Antiandrogen monotherapy is used more frequently than the LHRH agonists.
 - c. Hormonal therapy is being used as primary therapy in patients with high-risk prostate cancer
 - d. a and b
 - e. a and c
7. Which two factors are important determinants of the pattern (local or systemic) of recurrence?
 - a. PSA kinetics
 - b. Primary disease characteristics
 - c. Primary therapy received
 - d. a and b
 - e. a and c
8. In men concerned about maintaining sexual function, which of the following hormonal therapies would be an alternative at the time of biochemical recurrence?
 - a. Goserelin
 - b. Bicalutamide
 - c. Leuprolide
 - d. DES
 - e. All of the above
9. Clinical trials have demonstrated that adjuvant hormonal therapy is equivalent to hormonal therapy given at the time of biochemical recurrence.
 - a. True
 - b. False
10. Extended pelvic lymphadenectomy is associated with a high rate of lymph node metastasis outside of the fields of standard lymphadenectomy, in cases of clinically localized prostate cancer.
 - a. True
 - b. False

11. Data suggest which of the following drugs may prevent or reverse some or all bone mineral density associated with androgen deprivation therapy:

- a. Taxanes
- b. Hormonal therapies
- c. Bisphosphonates

d. Anthracyclines
12. Based on the 2001 Urology article by Amling et al, obese prostate cancer patients:

- a. Present for radical prostatectomy at a younger age
- b. Present with higher mean Gleason scores
- c. Present with a lower percentage of organ-confined cancers

Post-test Answer Key: 1. a, 2. b, 3. e, 4. d, 5. b, 6. e, 7. d, 8. b, 9. b, 10. a, 11. c, 12. d

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5 = Outstanding 4 = Good 3 = Satisfactory 2 = Fair 1 = Poor

Extent to which program activities met the identified objectives

Upon completion of this activity, participants should be able to:

- Discuss how to use antiandrogen withdrawal as an intervention for prostate cancer patients progressing on combined androgen blockade. 5 4 3 2 1
- Explain the rationale for monitoring patients with elevated PSAs and 2 negative biopsies, rather than obtaining further biopsies. 5 4 3 2 1
- Compare the treatment trends in CaPSURE to one's own management of prostate cancer patients. 5 4 3 2 1
- Describe how to counsel prostate cancer patients about the timing and choice of hormonal therapy. 5 4 3 2 1
- Explain the staging and therapeutic implications of extended pelvic lymphadenectomy in patients undergoing radical prostatectomy. 5 4 3 2 1
- Identify the effects of androgen deprivation therapy on bone and possible interventions in prostate cancer patients. 5 4 3 2 1
- Review the relationship between obesity and race in predicting adverse pathologic variables in patients undergoing radical prostatectomy. 5 4 3 2 1

Overall effectiveness of the activity

- Objectives were related to overall purpose/goal(s) of activity 5 4 3 2 1
- Related to my practice needs 5 4 3 2 1
- Will influence how I practice 5 4 3 2 1
- Will help me improve patient care 5 4 3 2 1
- Stimulated my intellectual curiosity 5 4 3 2 1
- Overall quality of material 5 4 3 2 1
- Overall, the activity met my expectations 5 4 3 2 1
- Avoided commercial bias or influence 5 4 3 2 1

Will the information presented cause you to make any changes in your practice?

___ Yes ___ No

If Yes, please describe any change(s) you plan to make in your practice as a result of this activity.

Degree:

- MD DO PharmD RN NP PA BS Other _____

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U P D A T E

Editor

Neil Love, MD

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Michelle Finkelstein Paley, MD
Richard Kaderman, PhD

Writers

Lilliam Sklaver Poltorack, PharmD
Jennifer Motley, MD
Sally Bogert, RNC, WHCNP
Douglas Paley

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Frank Cesarano

Technical Services

Arly Ledezma

Production Coordinator

Cheryl Dominguez

Editorial Assistants

Patricia McWhorter
April Marcus
Tere Sosa

Contact Information

Neil Love, MD
Director, Physician and
Community Education
NL Communications, Inc.
University of Miami
Conference Center
400 SE Second Avenue
Suite 401
Miami, Florida 33131-2117

Fax: (305) 377-9998

E-mail:

nlove@med.miami.edu

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